The following colorectal cancer research updates extend from April 12th, 2018 to June 8th, 2018 inclusive and are intended for informational purposes only.

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### DRUGS / SYSTEMIC THERAPIES

1. **Risk of recurrence in stage III colon cancer according to RAS- and BRAF-mutation status (May 25/18)**

In a study reported in *JAMA Oncology*, investigators from the Université Paris Descartes found that the risk of recurrence among patients with stage III colon cancer differed for the primary tumour location depending on RAS- and BRAF- mutation status. In the study, 2,559 patients were randomly assigned to receive adjuvant FOLFOX (leucovorin, fluorouracil, and oxaliplatin) with or without cetuximab (Erbitux). 1,900 patients were screened with genetic sequencing, and the primary tumour location was identified in 1,869. 57% of patients were male, 40% had a right-sided tumour, 50% had RAS mutations, and 11% had BRAF mutations. In the investigators’ analysis, no significant difference in disease-free survival was found between right-sided and left-sided tumours. It was determined, however, that survival *after recurrence* and overall survival were better for left-sided tumours compared to right-sided tumours, with 5-year rates of 31.1% vs. 18.5% and 84.2% vs. 78.6%, respectively. A trend toward better disease-free survival for right-sided tumours was observed among patients with BRAF mutations. In conclusion, the investigators suggest that while right-sided tumour location is associated with poor survival in patients with metastatic colon cancer as previously known, the link with disease recurrence appears to be far more variable among patients with stage III colon cancer and RAS or BRAF mutations compared to wild type.


2. **Soy lecithin NSAID combo drug protects against cancer with fewer side effects, UTHealth reports (May 29/18)**

Researchers from the University of Texas Health Science Center found that when a chemical extracted from soybeans was combined with a non-steroidal anti-inflammatory drug (NSAID), the anticancer properties of the drug were augmented with a simultaneous reduction of side effects. The NSAID indomethacin in combination with phosphatidylcholine also known as soy lecithin, was studied head-to-head with three other NSAlDs, including aspirin. The specific combination of indomethacin with soy lecithin resulted in the least gastrointestinal bleeding (the most common side effect of prolonged NSAID use) with superior colorectal cancer (CRC) protection. NSAlDs function by decreasing the production of substances in the body that promote inflammation and have been shown to be protective against heart disease, arthritic pain and CRC. As many cancers thrive in an inflammatory state in the body, a potential role has arisen for NSAlDs in cancer therapy. This novel combination of an NSAID with soy lecithin to reduce side effects of the drug are a potential leap forward in the use of NSAlDs for cancer prevention and treatment.


[https://www.sciencedaily.com/releases/2018/05/180529185340.htm](https://www.sciencedaily.com/releases/2018/05/180529185340.htm)

3. **Phase I study of Cobimetinib with Bevacizumab and Atezolizumab for colorectal cancer (Mar 30/18)**

In this non-randomized phase I trial, the safety, tolerability and pharmacokinetics of cobimetinib in combination with atezolizumab and bevacizumab among patients with metastatic colorectal cancer will be evaluated. Cobimetinib is an oral MEK kinase inhibitor which targets cell signalling involved in cell division and growth. Atezolizumab is an anti-PD-L1 antibody which targets the PD-L1 and PD-1 receptor to prevent suppression of the immune system against cancer cells. Bevacizumab is an antibody which interferes with the process of new blood vessel formation (angiogenesis) in cancer cells. All patients will have received at least 1 previous therapy with fluoropyrimidine and oxaliplatin or irinotecan. Cobimetinib will be administered orally while atezolizumab and bevacizumab will be given intravenously. In the first stage of the trial, patients will receive the drug combination until the disease progresses, unacceptable toxicity or withdrawal from the trial. In the second stage of the trial, the patients will be divided into two groups. The first group will receive the drug combination and undergo repeated tumour biopsy. The second group will receive atezolizumab and bevacizumab plus the cobimetinib dose that was given in stage I. For more information regarding the study, including inclusion and exclusion criteria, locations and contact information, visit: [https://ClinicalTrials.gov/ct2/show/NCT02876224](https://ClinicalTrials.gov/ct2/show/NCT02876224). The study is open and recruiting patients as of Oct 24, 2017 in the U.S., U.K., and Spain.


4. **Cell type switch helps colon cancer evade treatment, study suggests (May 16/18)**
German researchers have discovered that colorectal cancers (CRC) are often resistant to existing drug treatments because they are made up of two different cell types that can replace one another when one cell type is killed. The study suggests that combination therapies which target both cell types may be more effective at treating CRC, which continues to be the third most common cause of cancer death in the world. Currently, while early-stage CRC can be surgically removed, later stages of the disease demand more targeted treatments, such as therapies to block the MAPK pathway that stimulates cancer cell progression. Targeting MAPK signalling has only shown limited effects and normally prolongs survival by only a few months. One alternative is to target the NOTCH signalling pathway, which is also believed to drive CRC progression. Initial trials of NOTCH pathway inhibitors, however, have yielded disappointing results. The German research team examined over 300 patient samples and found that NOTCH pathway signalling was not turned on in all CRC cells. Cells in the centre of tumours demonstrated signs of active NOTCH signalling but reduced MAPK activity. This particular group of cells appeared to proliferate very rapidly. In contrast, cells at the edge of the colorectal tumour showed high levels of MAPK signalling but little NOTCH signalling activity. While this cell population at the tumour edge proliferated less rapidly, it appeared to be undergoing the beginning stages of metastasis, whereby cancer cells invade and spread to other tissues of the body. When these two cell types were studied in mouse models, the tumours quickly lost their MAPK-active cells when treated with the MAPK pathway inhibitor selumetinib. The number of NOTCH-active cells, however, appeared to increase, compensating for the loss of the MAPK-active cells. Furthermore, after stopping selumetinib treatment, some of the NOTCH-active cells gave rise to new MAPK-active cells at the tumour edge. When treated with NOTCH pathway inhibitor dibenzazepine, NOTCH-active cells were eliminated but the population of MAPK-active cells grew and gave rise to new NOTCH-active cells once the treatment with the inhibitor was complete. Researchers concluded that CRCs may actually evade targeted treatment against MAPK or NOTCH pathways by shifting interchangeable from one pathway to another. When two inhibitor therapies were combined, a strong repressive effect on the tumour cell proliferation as well as increased cell death were observed, resulting in slowed tumour growth and longer survival times compared to either treatment alone.

5. Every bowel tumour and bowel cancer cell has unique genetic fingerprints (Apr 11/18)

Researchers from the Wellcome Sanger Institute in the Netherlands have used the latest single cell and “organoid” technologies to better understand the mutation process of colorectal cancer (CRC). The team studied tissue from three patients with CRC, taking normal stem cells from the colon and cells from four different areas of their tumours. They grew these cells into “organoids” or “mini-colons” in the laboratory to amplify the tumour cells so they could be better studied. Until now, it has not been possible to study single cells from tumours and normal tissue to get an accurate idea of how these cells behave. With organoid technology, researchers are able to study each cell type without the errors that standard single cell methods bring. A far more comprehensive comparison of individual normal and tumour cells from the exact same type of tissue taken at the same time from the same person was possible to better understand how the cancer had developed. They found that the tumour cells had far more mutations than normal cells, and that not only was each CRC very genetically different, but each cell that was studied within that cancer was different. This incredible genetic diversity among tumours seemed to be a general feature of CRC. The mutation rate of the tumours appeared to start many years before the cancer was diagnosed. This timeframe could help to provide diagnostic clues in the future if a method could be developed to detect when the mutation rate begins to rise in the cell. By studying the patterns of mutations from individual healthy and tumour cells, it is possible to know what mutational processes have occurred and then dig deeper to see what has caused them. A better understanding of the origin of these processes could help to pinpoint new risk factors to help reduce the incidence of CRC, and also develop drugs to directly target specific mutational processes during CRC development.

6. New trigger for onset of colon cancer: may lead to better therapies (Apr 2/18)

The APC protein is known for its important role in the prevention of colorectal cancer (CRC). When APC activity is turned off, the development of CRC is triggered. 80% of CRCs are linked to the inactivation of the APC protein. Researchers from Vanderbilt University have found a new role for the APC gene in actually inhibiting several CRC activators. APC functions in a pathway that facilitates cell communication. When APC is inactive, cell communication is compromised, allowing for cell proliferation to occur without inhibition. Recent research has demonstrated that APC not only functions as a “brake” on cell proliferation, but also functions to control other activators in the same pathway. APC’s role in controlling various activators could open doors to new therapeutic targets. The finding that APC has new roles could help researchers better understand why APC mutations are more prevalent in certain cancers and not others. Certain tissues may have another mechanism as back-up to put the brake on cell proliferation when APC is mutated.

APC plays a role in the control of abnormal epithelial cell proliferation.

Image source: http://www.pnas.org/content/115/23


7. Hepatic Artery Infusion Pump (HAIP) Chemotherapy Program – Sunnybrook Odette Cancer Centre (Mar 20/18)

The HAIP program is a first-in-Canada for individuals where colon or rectal cancer (colorectal cancer) has spread to the liver and cannot be removed with surgery. The program involves a coordinated, multidisciplinary team approach to care, with close collaboration across surgical oncology, medical oncology (chemotherapy), interventional radiology, nuclear medicine, and oncology nursing. The Hepatic Artery Infusion Pump (HAIP) is a small, disc-shaped device that is surgically implanted just below the skin of the patient and is connected via a catheter to the hepatic (main) artery of the liver. About 95 percent of the chemotherapy that is directed through this pump stays in the liver, sparing the rest of the body from side effects. Patients receive HAIP-directed chemotherapy in addition to regular intravenous (IV) chemotherapy (systemic chemotherapy), to reduce the number and size of tumours. Drs. Paul Karanicolas and Yooj Ko are the program leads and happy to see patients eligible for the therapy.

Presently at Sunnybrook Odette Cancer Centre, HAIP is being used in patients with colorectal cancer that has spread to the liver that cannot be removed surgically and has not spread to anywhere else in the body. Patients who have few (1-5) and very small tumors in the lungs may be considered if the lung disease is deemed treatable prior to HAIP. If you believe you may benefit from this therapy and/or would like to learn more about the clinical trial, your medical oncologist or surgeon may fax a referral to 416-480-6179. For more information on the HAIP clinical trial, please click on the link provided below.

http://sunnybrook.ca/content/?page=colorectal-colon-bowel-haip-chemotherapy
8. Use of heated chemotherapy during surgery does not improve colorectal cancer survival (June 4/18)

The results from the phase III PRODIGE 7 trial presented at the ASCO Annual Meeting demonstrated that the addition of hyperthermic intraperitoneal chemotherapy (HIPEC) to surgical resection did not provide a survival benefit for patients with metastatic peritoneal colorectal cancer (CRC). Furthermore, long-term adverse events occurred more frequently with HIPEC than without. The study was the first to examine the role of HIPEC in combination with surgical resection for CRC in the peritoneum. About 20% of patients with metastatic CRC have metastasis to the lining of the peritoneum. When used in combination with surgery, HIPEC has been shown to increase survival compared with systemic chemotherapy alone. In this study, HIPEC was oxaliplatin based, heated to 43 degrees Celsius in order to increase the efficacy of the therapy. 265 patients (median age 60 years) with stage IV CRC and peritoneal metastasis were included in the study. Patients were randomly assigned to receive surgery plus HIPEC or surgery alone. The majority of patients underwent systemic chemotherapy before surgery, after surgery, or both. At median follow-up of 64 months, median overall survival (OS) was 41.2 months in the surgery arm, compared to 41.7 months in the HIPEC arm. There were no significant differences between OS between the two arms. Initially, researchers observed no differences in the rate of adverse events during the first 30 days. However, adverse events nearly doubled at 60 days in the HIPEC arm compared to the surgery arm alone (24.1% s. 13.6%). The researchers observed a survival benefit with HIPEC specifically among patients with a medium amount of disease in the peritoneal cavity.

Image source: https://en.wikipedia.org/wiki/Hyperthermic_intraperitoneal_chemotherapy

Quenet F, et al. LBA3503. Presented at: ASCO Annual Meeting; June 1-5, 2018; Chicago.


9. Living donor liver transplantation for unresectable colorectal cancer liver metastases (Jun. 1/18)

Approximately half of all colorectal cancer (CRC) patients develop metastases, commonly to the liver and lung. Surgical removal of liver metastases (LM) is the only treatment option, though only 20-40% of patients are candidates for surgical therapy. Surgical therapy adds a significant survival benefit, with a 5-year survival after liver resection for LM of 40-50%, compared to 10-20% 5-year survival for chemotherapy alone. Liver transplantation (LT) would remove all evident disease in cases where the colorectal metastases are isolated to the liver but considered unresectable.
While CRC LM are considered a contraindication for LT at most cancer centers, a single center in Oslo, Norway demonstrated a 5-year survival of 56%. A clinical trial sponsored by the University Health network in Toronto will offer live donor liver transplantation (LDLT) to select patients with unresectable metastases limited to the liver and are non-progressing on standard chemotherapy. Patients will be screened for liver transplant suitability and must also have a healthy living donor come forward for evaluation. Patients who undergo LDLT will be followed for survival, disease-free survival and quality of life for 5 years and compared to a control group who discontinue the study before transplantation due to reasons other than cancer progression.

https://clinicaltrials.gov/ct2/show/NCT02864485

**RADIATION THERAPIES/INTERVENTIONAL RADIOLOGY**

10. Study Offered at the Odette Cancer Centre to Treat Recurrent Rectal Cancer (Jun 1/18)

Magnetic resonance-guided focused ultrasound (MRg-FU) is a non-invasive, outpatient modality being investigated for the thermal treatment of cancer. In MRg-FU, a specially designed transducer is used to focus a beam of low intensity ultrasound energy into a small volume at a specific target site in the body. MR is used to identify and delineate the tumour, focus the ultrasound beam on the target and provide real-time thermal mapping to ensure accurate heating of the designated target with minimal effect to the adjacent healthy tissue. The focused ultrasound beam produces therapeutic hyperthermia (40-42°C) in the target field causing protein denaturation and cell damage. Currently, there is no prospective clinical data reported on the use of MRg-FU in the setting of recurrent rectal cancer. Recurrent rectal cancer is a vexing clinical problem. Current retreated protocols have limited efficacy. The addition of hyperthermia to radiation and chemotherapy may enhance the therapeutic response. With recent advances in technology, the investigators hypothesize that MRg-FU is technically feasible and can be safely used in combination with concurrent re-irradiation and chemotherapy for the treatment of recurrent rectal cancer without increased side-effects. The study is being offered at the Odette Cancer Centre. Here is the link to the study protocol:

https://clinicaltrials.gov/ct2/show/NCT02528175?term=magnetic+resonance+guided+focused+ultrasound&recr=Open&rank=1

**SCREENING**

11. Study confirms curable state between single and widespread cancers (May 7/18)

23 years ago, two Chicago-based cancer specialists suggested that there existed an intermediate state between curable localized cancers and lethal metastatic disease. They labelled this state “oligometastasis” – “a few that spread” in Greek. In their studies, they focused on cancer cells that had spread from a primary tumour in the colon or rectum to a few distant sites. They also suggested, among great controversy, that many of these patients with metastatic disease, depending on their disease burden, could be cured with surgery or targeted radiation therapy.
alone. Today, these two specialists have confirmed their oligometastasis hypothesis and have succeeded in identifying molecular patterns to predict which patients are most likely to benefit from surgery and long-term survival. The researchers described results from 134 patients with a median age of 61 with cancer of the colon (72%) or rectum (28%) with liver metastases. The patients were treated with perioperative chemotherapy (5-flourouracil based) and proceeded with surgical removal of all detectable signs of cancer that had spread to the liver. For each patient, DNA sequencing, RNA sequencing, microRNAs and microsatellite instability testing was performed. The data sorted patients into three different tumour subtypes based on molecular analysis. Group 2 was found to have the highest 10-year survival rates compared to groups 1 and 3. More in depth examination revealed that subtype 2 tumours seemed to trigger an immune response that helped stem the rate of further tumour proliferation. These subtype 2 tumours were then reclassified and combined with clinical data from patients with these tumours. Researchers were able to predict a vast difference in survival – subtype 2 had a 94% chance of 10-year survival, while subtypes 1 and 3 had 10-year survivals of 45% and 19%, respectively. The researchers’ findings were able to provide a more detailed framework for the classification and treatment of metastasis, with the study being the first of its kind to combine clinical and molecular data to make better disease predictions. The findings have great potential to improve the treatment and outcome of patients with colorectal liver metastases.

12. Top-down approach gets to the bottom of cancer (Apr 17/18)

For the first time, a research team from Northwestern University has characterized a fully intact protein that results from the mutation of the RAS gene – the first cancer gene ever identified in human cancer cells. To date, researchers have typically examined RAS proteins by cutting them up and analyzing the pieces, which is a limited approach as they inevitably must be put back together to be fully understood. A piece of a given protein will behave completely differently than its whole. When a RAS gene is functioning normally, it serves as an on/off switch in the cell to control cell proliferation. When RAS is mutated, the switch remains in the “on” position, allowing cells to divide uncontrollably and eventually leading to cancer. The RAS mutation accounts for 30% of all human cancers, including 95% of pancreatic and 45% of colorectal cancers. Currently, no drugs exist which target the mutation to fix the broken “switch”, and RAS-related cancers remain notoriously difficult to treat – standard chemotherapy and radiation therapies have been proven to be largely ineffective. The team from Northwestern’s Proteomics (the study of proteins) Center of Excellence has developed a new technology that can precisely detect and quantify the effect of RAS mutations and the RAS proteins for which they code. A better understanding of the RAS proteins and how they function in cancer could open new potential pathways for treatment. Using “top-down” proteomics, i.e. studying the mutated protein first and then observing its impact on cancer development, the team was able to study proteins while they are still fully intact. The technology was applied to KRAS, one member of the RAS gene family. The scientists observed the presence of KRAS protein in colorectal cancer cell lines and analyzed how much it changed compared to healthy tissues. They were able to then understand how the KRAS proteins look in different tumours and better characterize the cancer. New knowledge of cancer proteins could lead to new opportunities in advancing treatment strategies against cancer.
13. New guidelines recommend earlier colorectal cancer screening (May 31/18)

New proposed guidelines from the American Cancer Society (ACS) recommend that screening for colorectal cancer (CRC) for average-risk adults start at 45 years of age, five years sooner than the previous recommendation. The change to the recommendation is based on growing evidence that demonstrates increasing incidence of CRC among younger adults. Among adults below the age of 55 years, there was a 51% increase in the incidence of CRC from 1994 to 2014 and an 11% increase in deaths from 2005 to 2015. In contrast, CRC incidence has declined steadily over the past twenty years among people 55 and older, due in part to better screening that removes potentially malignant polyps. A recent study found that adults born around 1990 have twice the risk of CRC and four times the risk of rectal cancer compared to adults born around 1950, who currently have the lowest risk. Studies indicate that the increased risk that younger people have for CRC will remain as they age. The current options for CRC screening are annual fecal immunochemical testing; annual high-sensitivity, guaiac-based fecal occult blood test; multitarget stool DNA testing every 3 years; colonoscopy every 10 years; computed tomography colonography every 5 years; and flexible sigmoidoscopy every 5 years. All positive results on non-colonoscopy screening tests should be promptly followed up with a colonoscopy. The ACS guideline committee has also developed new materials to help facilitate conversations between clinicians and patients to help patients select the screening test best suited to their needs. It is important to note that the new guidelines apply to average risk individuals. Those at high risk for CRC, including those with a family history of the disease, a personal history of inflammatory bowel disease or polyps diagnosed before the age of 60, should discuss their risk and the appropriate screening with their clinician. Adults in good health should continue CRC screening until the age of 75 years, at which the decision to continue screening should be personalized based on the patient’s preferences, overall health, life expectancy and screening history. With hope, the widespread adoption of the new guidelines will have a positive impact on the incidence, suffering, and mortality caused by CRC.


https://www.sciencedaily.com/releases/2018/05/180531162314.htm

14. X-ray capsule shows efficacy for prep-free colon cancer screening (May 31/18)

C-Scan is a novel X-ray imaging capsule that can accurately visualize colon polyps without the normal bowel cleansing preparation, a major barrier to colorectal cancer (CRC) screening uptake. Results from a multi-center clinical study of C-Scan demonstrate that the capsule is safe, and can correctly identify polyps with the majority of the colon imaged. The risk of false positives, or false polyp identification has been shown to be consistently low. In the study, 45 patients underwent the capsule screening, as well as a fecal immunochemical test (FIT) to compare the sensitivity and specificity of polyp detection with both procedures. Afterward, investigators performed colonoscopies on the patients to confirm polyp detection. The C-Scan capsule had 45% sensitivity in detecting polyps compared to 37% for FIT. The capsule’s sensitivity increased to 78% when more than half of the colon surface was imaged and 100% with more than 70% imaging. Specificity was 90% in the group with 50% of the colon surface imaged and 86% in the group with 70% of the colon surface imaged. The study data demonstrate the capsule’s safe passage through the gut, ultra-low radiation exposure and the ability to identify abnormal growths in the colon without the need for any bowel preparation.

The C-Scan X-ray capsule.

Image source: https://www.israel21c.org/high-tech-capsule-could-be-alternative-to-colonoscopy/

https://www.healio.com/gastroenterology/therapeutics-diagnostics/news/online/%7b674b6e6-3b63-4ebc-bd43-465f4fa711f6%7d/x-ray-capsule-shows-efficacy-for-prep-free-colon-cancer-screening

15. A new, streamlined approach to diagnosing and treating bowel cancer (Apr 17/18)

New research from the University of Adelaide in Australia has discovered a more rapid and cost-effective method to determine which DNA mutations are responsible for colorectal cancer (CRC). With new gene editing technology, the researchers were able to take different DNA changes and engineer them into the normal colon tissue in rapid time.
speeding up the research process by cutting off years of traditional laboratory experiments. The growing cancers can then be observed in the research institute’s imaging centre via colonoscopy, CT and PET scan. The method allows researchers to determine which DNA changes are important to the development of the cancer. The outcomes of these specific DNA mutations on colon tissue can now be observed in a quarter of the time, thereby increasing the speed at which results reach the patient at a fraction of the cost and using far fewer animal test subjects. The technology allows scientists to screen and repurpose existing drugs which may not have been tested in CRC and improve CRC detection by being able to actually watch the cancer develop in real time. Researchers are hoping that the new technology will help to develop new drug targets and be able to deliver them to patients faster than through the traditional methods.


16. Cognitive behavioural therapy, acupuncture reduce insomnia among cancer survivors (May 16/18)

According to a new study presented at the ASCO Annual Meeting, moderate to severe insomnia improved among cancer survivors after cognitive behavioural therapy (CBT) or acupuncture. Among cases of mild insomnia, CBT appeared more effective than acupuncture. Insomnia is a very common condition among as many as 60% of cancer survivors, having an important impact on quality of life. CBT for insomnia is a very effective therapy and considered the gold standard of treatment, though it is not widely accepted. It is a very specialized kind of therapy that is not available at many cancer centres. Acupuncture is another treatment that can be used to improve pain and sleep problems. The study aimed to determine which therapy is more effective in treating insomnia among survivors. 160 cancer survivors with clinically diagnosed insomnia disorder were evaluated. Patients received either acupuncture via stimulation of different body points with needles or CBT, which consisted of relaxation training, sleep restriction, stimulus control, cognitive restructuring and education. The interventions lasted an 8-week period. At baseline, 33 survivors had mild insomnia, 94 had moderate insomnia and 33 had severe insomnia. Severity of insomnia was determined by the Insomnia Severity Index. Patients who received acupuncture experienced an 8.3 point reduction in insomnia severity compared to a 10.9 point reduction among patients who received CBT. A greater proportion of patients with mild insomnia responded to CBT compared to acupuncture. Patients with moderate to severe insomnia showed similar responses to both CBT and acupuncture. Improvements in insomnia severity continued up to the 20-week follow-up. Both groups experienced similar improvements to quality of life for physical and mental health. In conclusion, alternative treatments such as acupuncture and CBT are effective methods for treating insomnia among cancer survivors and improving quality of life.


17. Candirect research study: Learn more about a study for patients who have completed their cancer treatments and are experiencing low mood (Apr 1/18)

15% of cancer survivors are estimated to experience mood problems even one year post-treatment. The CanDirect research study aims to support cancer survivors with mood problems by providing study participants with a self-care toolkit designed to help users better manage their mood and anxiety as well as phone coaching for a maximum duration of 6 months. Participation is open to eligible adult survivors residing in Quebec and Ontario who have completed cancer treatment for a non-metastatic cancer and who are experiencing depressive symptoms. For additional information, please click on the following link:

18. Colorectal cancer in younger patients develops via different genetic pathway (May 29/18)

Based on recent research presented at the American Society of Colorectal Surgeons Annual Scientific Meeting, patients below the age of 50 years that are diagnosed with colorectal cancer (CRC) were less likely to develop cancer through the serrated polyp pathway, which is more common in older patients. The difference in biology helps to explain why CRC is predominantly distributed in the left side of the colon and rectum in younger patients and appears to arise from a particular genetic pathway apart from the methylation pathway common among older patients. In the study, tumour biology was compared between patients below the age 50 with those older than 50. CRC samples from a tumour bank were reviewed and each was checked for cpG island methylator phenotype (CIMP) and KRAS and BRAF mutations. Of the 497 cancers observed, 11.5% were from patients below the age of 50. None of the cancers were hypermethylated as was observed in 22% of the cancers from older patients (>50 years). With each decade of age at diagnosis, an increase in the proportion of CIMP-high cancers was observed. While none of the younger patients had BRAF mutations, 10.6% of the older patients did. KRAS mutations were also found to be less common in younger patients compared to older patients (22.8% vs. 30.7%, respectively). With respect to tumour location, tumours among younger patients were less likely to be centrally located compared to the older group. In concordance with other research, a higher prevalence of left-sided and rectal cancers was observed in younger patients, suggesting that people in their 40s may benefit from adapted screening techniques such as flexible proctosigmoidoscopy which can reach these areas.


https://www.healio.com/gastroenterology/oncology/news/online/%7b8d43a564-56ad-4872-9a2d-12a506c445e%7d/colorectal-cancer-younger-patients-develops-via-different-genetic-pathway

19. Young adult colorectal cancer clinic available at Sunnybrook (Mar 18/18)

A recent study led by University of Toronto doctors has observed a rise in colorectal cancer rates in patients under the age of 50. The study mirrors findings from the U.S., Australia and Europe. The growing colorectal cancer rates in young people come after decades of declining rates in people over 50, which have occurred most likely due to increased use of colorectal cancer screening (through population-based screening programs) which can identify and remove precancerous polyps. Patients diagnosed under the age of 50 have a unique set of needs, challenges and worries. They are unlike those diagnosed over the age of 50. Dr. Shady Ashamalla (colorectal cancer surgical oncologist), and his team at the Sunnybrook Health Sciences Centre understand the needs of this patient population.

Dr. Ashamalla belongs to a multidisciplinary team of experts in the Young Adult Colorectal Cancer Clinic who will work with young colorectal cancer patients, regardless of disease stage, to create an individualized treatment plan to support each patient through their cancer journey. Their needs and concerns will be addressed as they relate to:

- Fertility concerns and issues
- Young children at home
- Dating/intimacy issues
- Challenges at work
- Concerns about hereditary cancer
- Relationships with family and friends
- Psychological stress due to any or all of the above

The team of experts consist of:

- Oncologists (medical, surgical, radiation)
- Social workers
- Psychologists
- Geneticists
• Nurse navigator
Should a patient wish to be referred to Sunnybrook, they may have their primary care physician or their specialist refer them to Sunnybrook via the e-referral form which can be accessed through the link appearing below. Once the referral is received, the Young Adult Colorectal Cancer Clinic will be notified if the patient is under the age of 50. An appointment will then be issued wherein the patient will meet with various members of the team to address their specific set of concerns.

http://sunnybrook.ca/content/?page=young-adult-colorectal-cancer-clinic

NUTRITION/ HEALTHY LIFESTYLE

20. Four years post-treatment, exercise improves physical activity levels, reduces fatigue in patients with breast and colon cancers (Apr 10/18)

A recent follow-up to the PACT study determined that a physical exercise intervention conducted during adjuvant chemotherapy improved overall physical activity levels when measured 4 years after the beginning of treatment, with a reduction in fatigue among patients. The PACT study aimed to determine the benefits of a supervised exercise program on fatigue and physical fitness among patients with stage I to III breast or colon cancer undergoing chemotherapy after surgery. Fatigue related to cancer treatment can be among the most distressing side effects and may persist for many years after treatment is complete. At their 4-year follow-up, patients who had completed the 18-week exercise program as part of the PACT study were engaging in an average of 20 minutes more physical activity per day compared to those who were receiving usual care. These results are important as it is already known from related studies that regular physical activity after a breast or colon cancer diagnosis is linked to better disease outcomes. During the PACT study, positive short-term effects of the exercise intervention on fatigue were reported. The follow-up aimed to examine the durability of these effects several years post-treatment. The exercise intervention involved 60 minutes of moderate-to-high-intensity aerobic and strength training twice a week under the supervision of a physical therapist, in addition to 30 minutes of home-based physical activity 3 days a week. The program also involved cognitive behavioural elements that aimed to increase patients’ confidence and willingness to be and stay active even after the 18-week intervention was complete. The majority of the participants were female, with an average age of 50. At 4-year follow-up, patients in the intervention group reported 90 minutes a day of moderate to vigorous activity, compared to 70 minutes per day in the usual care group. While there was a trend towards less fatigue in the intervention group, the results were not statistically significant. These findings are important as they support the recommendation of regular exercise during cancer treatment to improve both short and long-term health effects.

http://www.ascopost.com/issues/april-10-2018/four-years-posttreatment-exercise/

21. Obesity inhibits key cancer defense mechanism (Apr 26/18)

While obesity is a known risk factor for promoting tumour growth and malignant progression in colon cancer, its role in cancer initiation has remained uncertain. Normally, the epithelial cells which line the surfaces of organs have the natural ability to sense potentially cancerous cells and push them out of their local environment through a process known as cell competition. Researchers at Hokkaido University in Japan used mice models expressing the known cancer-inducing mutant protein RAS. Potentially cancerous RAS-transformed cells are normally removed by epithelial cells. When the RAS mice were fed high-fat diets resulting in obesity, the epithelial cell defense mechanism was suppressed and the number of RAS-transformed cells remaining in the tissue increased. This suppression was observed in the colon and pancreas, but not in the lung. One month later, the RAS-transformed cells developed a tumour in the pancreas of mice fed a high-fat diet. These results support previous associations made between obesity and intestinal and pancreatic cancer, but not lung cancer. Further analyses in the study revealed that fatty acids and chronic inflammation stimulated the suppression of the defense mechanism. When the obese mice were treated with aspirin, known for its anti-inflammatory properties, the defense mechanism was significantly improved. This is the first study to demonstrate that obesity and chronic inflammation can influence competitive interactions between normal and mutated cells. Other factors that impact inflammation such as infection, smoking, and sleeping patterns may also have an impact on the suppression of the body’s intrinsic defense mechanism. In conclusion, maintaining a healthy lifestyle and body weight is crucial as we learn more and more about how obesity compromises our bodies natural defense mechanisms and puts us at increased risk of cancer and many other diseases.
22. Significant weight gain during puberty tied to colon cancer in men (May 25/18)

New research has shown that boys who are overweight with an above-average increase in BMI during puberty had a higher risk for developing colorectal cancer (CRC) in adulthood. BMI throughout childhood and adolescence may have an important role in determining CRC risk in later life. Researchers performed a study which included 37,663 Swedish men with childhood BMI data available, who were born between 1945 and 1961 and followed through 2013. BMI change during puberty was calculated by subtracting BMI at age 8 from BMI at age 20. Based on national registry data, 257 participants developed colon cancer and 159 developed rectal cancer in adulthood. An association was found between childhood BMI at age 8 and risk for colon cancer diagnosis – specifically, a significant interaction was found between childhood BMI and change in BMI during puberty with later colon cancer risk. More specifically, researchers found that childhood BMI was independently associated with CRC risk only among those who had a change in BMI above the median. Due to study limitations such as a lack of population diversity (study primarily involved white men), and the lack of data on factors such as BMI at later age and diet and exercise patterns, no firm conclusions about whether a significant change in BMI actually causes colon cancer could be made. The researchers concluded that overweight boys with a higher than median change in BMI during puberty have a 48% higher risk of developing colon cancer in adulthood. Such associations were not observed between changes in BMI and incidence of rectal cancer.


https://www.healio.com/gastroenterology/oncology/news/online/%7b8576e80-e2bc-460f-aed9-37005f123f57%7d/significant-weight-gain-during-puberty-tied-to-colon-cancer-in-men?nc=1

23. How to use food as medicine to prevent, reverse chronic diseases (Apr 20/18)

A presentation at the American College of Physicians Internal Medicine Meeting stressed the importance of a healthy diet in the prevention and reversal of chronic diseases such as cardiovascular disease, diabetes, cancer and obesity. Nearly half of all deaths due to heart disease, stroke and diabetes are directly linked to poor, suboptimal diet. The impact of poor diet on mortality from chronic conditions is actually greater than that of smoking. While many patients know that it is not a good idea to smoke, many probably do not have an idea of just how important the food choices are that they make each day. Through a change in lifestyle habits, particularly nutrition, there is the possibility to prevent about 80% of chronic disease incidence.
Foods and eating patterns can be classified into three different categories: healthful, debatable and unhealthful. Foods labeled as healthful include whole grains, legumes, fruits and vegetables, nuts and seeds, and have a general consensus on their ability to promote health and prevent disease. Foods labeled as unhealthful, including processed meats, red meat, refined sugar and grains, and ultra-processed foods have a general consensus that they cause harm to the body. Foods labeled as debatable, including poultry, eggs, dairy and fish, have shown both benefits and harms.

With respect to cancer incidence, consuming 100 grams of red meat per day increases the risk of colorectal cancer by 17% and 50g of processed meat per day increases the risk by 18%. A consumption of seven and a half servings of fruit and vegetables per day is associated with a significant 14% reduction in total cancer risk. Whole grains are also powerful cancer-fighting foods, reducing CRC risk and total cancer mortality by 17%. Physicians at the meeting reinforced the fact that no dramatic changes in eating patterns can happen overnight. It is important not to rely only on one’s willpower to avoid unhealthy foods and eat healthy foods, but rather, it may be necessary to change one’s environment and routine and form new healthy habits that can be sustained.


https://www.sciencedaily.com/releases/2018/04/180430160421.htm

24. Identifying the mechanism in obesity’s link to colon cancer (Apr 30/18)

New study findings from the University of Massachusetts Amherst report that a new molecular mechanism has been identified which helps to explain the link between obesity and increased risk of colon inflammation, a major factor in colorectal cancer (CRC) development. Using mouse models, the research team found that the inhibition of an enzyme known as soluble epoxide hydrolase, sEH, could significantly reduce the risk of obesity-induced colon inflammation. Currently in the US, more than one third of adults are obese, a condition which increases one’s risk of developing CRC by 30-60%. Colon inflammation is an early warning sign of CRC, and the study demonstrated why and how obesity increases this risk. Using techniques to analyze the lipid metabolic profiles in the colon of groups of lean and obese mice, the concentration of sEH-produced metabolic products was found to be higher in the colons of obese mice. This suggested that sEH is over-expressed in the colons of obese mice and in involved in obesity-induce colon inflammation. Blocking the expression of the enzyme prevented the mice from developing colon inflammation, even among mice fed a high-fat diet. The study results provide useful insight into the potential for sEH inhibitors in the prevention of colon inflammation and CRC.

25. A Phase III study on the impact of a physical activity program on disease-free survival in patients with high risk stage II or stage III colon cancer: a randomized controlled trial (CHALLENGE) (Mar 15/18)

The purpose of this study is to compare the disease-free survival of patients involved in a physical activity program (designed to increase physical activity participation) who also receive general health education materials (about diet and physical activity) to patients who receive the general health education materials only. This study is being done because, as of yet, there is no conclusive evidence that physical activity will decrease the likelihood of colon cancer recurrence. This study will also obtain important information about the impact of physical activity on patients’ physical functioning, body composition, quality of life, fatigue, mood, cytokines and the insulin pathway, and their influence on prognosis, as well as cost-effectiveness.

Eligibility: Medically fit colon cancer patients (high risk stage II and stage III) who have completed adjuvant chemotherapy within the past 60-180 days. Current physical activity levels must not meet the recommended guidelines (>150 minutes of moderate-to-vigorous or >75 minutes of vigorous exercise/week). Following registration, and prior to randomization, patients must successfully complete at least two stages of a submaximal exercise test to ensure they are able to safely exercise at a moderate to vigorous intensity.

Participation: Limited to invited centres. For more information, visit the link below: https://scooby.ctg.queensu.ca/tum_bank/tum.php?g_cmd=trial_info&g_trial_cd=CO21

26. High dose Vitamin D supplementation in Stage 4 Colorectal Cancer Patients (Mar 18/18)

A large body of evidence suggests that high blood levels of Vitamin D decreases the risk of developing cancer, especially colorectal cancer. Very little is known about what role optimum blood levels of Vitamin D can play in the treatment of cancer. The purpose of this clinical trial is to study the therapeutic effect and the safety of high-dose vitamin D supplementation in stage 4 (metastatic) colorectal cancer patients. Who is eligible to participate? Anyone
who has a stage four colorectal cancer diagnosis, living in Ontario or British Columbia, may be eligible to participate. All participants need to have access to a Lifelabs facility for blood and urine collections. What is involved? This 40-month study involves regular lab tests and follow-up phone calls. Participation is fully voluntary, and participants may withdraw at any time. Participants will be randomized into either a high-dose vitamin D treatment group or a control group. Participants in both groups may continue all other cancer treatments including chemotherapy. Treatment group: Participants in the treatment group receive daily oral high-dose Vitamin D supplementation provided free of charge through the clinical study. They also receive daily calcium supplementation 1000mg daily as per guidelines, provided free through the clinical study. Participants will have monthly blood and urine tests for monitoring purposes. All laboratory tests are free of charge. Participants also need to be available for a 15-minute phone consultation with a study coordinator every 2 months. Control group: Participants in the control group will continue their usual amount of Vitamin D and/or calcium if they wish to do so. No supplements will be provided through the study. Participants will be asked to provide a small blood and urine sample at the beginning of the study, every 8 months and at the end of the study. These blood and urine tests will be free of charge. Contact person: If you have any further questions regarding this study or you are interested in participating in this study, please contact us: British Columbia: 604-734-7125, toll free 1-888-734-7125 or vitDstudy@inspirehealth.ca Ontario: 613-792-1222, toll free 1-855-546-1244 or research@oicc.ca